

Opioids, pain, and fear

Cancer pain has been described as ‘total pain’ presenting physical, psychological, social, and spiritual components [1], and can thus be defined as a ‘biopsychosocial experience’ [2]. It is very difficult to identify the specific ‘percentage’ of each of these components for a given value in a numerical scale of pain assessment although it has been reported that emotional and cognitive components seem to be proportionally more important in cancer pain than in noncancer pain [3]. As cancer pain is a multifactorial experience and is present together with numerous other symptoms, pain management within the context of palliative care plays an important role in the systematic control of symptoms [4]. In fact, global and continuous palliative interventions in patients bring about a substantial reduction in the dose of opioids used for cancer pain management [5]. Cancer pain must therefore be dealt with using a global approach which obviously includes the correct use of analgesics, especially opioids, from the early stages of disease onwards.

Cancer pain, affecting 50% of patients at any given disease stage and 75% of patients with advanced disease [6], has been studied and defined in relation to the following: causes (neoplastic disease 60%–80%, therapies 25%–20%, not associated with either disease or therapy 10%–5% in outpatients and hospitalized patients, respectively); physiopathological characteristics (nociceptive pain 50%–70%, neuropathic pain 10%–30%, mixed pain 20%–40%); intensity (severe pain in 30% of cases); and number of pain sites (one pain site 20%; 2–4 pain sites 60%; and >4 pain sites 20%) [2, 7, 8].

The basic therapeutic strategy for managing cancer pain, the three-step Analgesic Ladder, was designed by the World Health Organization (WHO). This approach was recently criticized because it advocates a therapeutic intervention based mainly on pain intensity, independently of physiopathological mechanisms of the pain itself (although it must be highlighted that different adjuvant drugs are recommended on the basis of pain typology). While a correct use of the WHO Analgesic Ladder results in successful pain management in 90% of patients [4], a number of studies, however, have also reported inadequate pain control in 40%–70% of patients [9, 10], resulting in the emergence of a new type of epidemiology, that of ‘failed pain control’, caused by a series of obstacles preventing adequate cancer pain management.

Barriers to a correct treatment of cancer pain have been identified in recent years, and the Agency for Health Care Policy and Research, in its ‘First National Clinical Practice

Guidelines on Cancer Pain’, classified them into three categories: system, professional, and patient barriers [11].

System barriers are represented by low priority given to cancer pain treatment and by legal and regulatory obstacles to the use of opioids for cancer pain. The cancer patient runs the risk of becoming an innocent victim of a war waged against opioid abuse and addiction if the norms regarding the two kinds of use (therapeutic or nontherapeutic) are not clearly distinct. Furthermore, health professionals may be worried about regulatory scrutiny and may opt not to use opioid therapy for this reason. System barriers can be internal, such as inadequate or late start-up of palliative care programmes, or external, such as regulatory excesses and complications. Finally, in developing countries, system barriers may also be represented by high cost of opioids, geographic dispersion, problems of availability of treatment or access to it, or by ‘opioid phobia’ [2, 12, 13].

It has been reported that physician barriers to correct cancer pain management consist of the following: use of a ‘disease-based’ rather than a ‘symptom-based’ model of care; lack of physician education and failure to follow existing guidelines; lack of priority given to symptom management; analgesia level on the basis of prognosis rather than severity of pain; fear of patient addiction and analgesic tolerance; poor assessment of pain and lack of proactive questioning about the symptom; insufficient experience of pain management (poor knowledge of opioid pharmacology, conversion, equianalgesia, rotation, doses, and ratio for breakthrough pain drugs); failure to use adjuvants; concern about and failure to treat opioid side-effects; failure to document information on drugs used, dosages given, timing, breakthrough pain, and laxatives administered; and failure to follow-up [2, 12].

Cherny’s study [14, 15] on European oncologists reported that a number of weaknesses emerged from a self-evaluation survey of their ability to manage symptoms of advanced disease and to collaborate with other health professionals. Rather surprisingly, a fairly low percentage of questionnaires, ~33%, were completed and returned. Only 43% of responders were regularly involved in the care of cancer patients at all stages of disease, including end-of-life care, 39% commonly coordinated meetings with the family of dying patients, and 11.8% managed delirium. With regard to palliative care, 42% reported that they had not received adequate training in this area, while 60.4% said they considered themselves to be reasonably skilled in palliative care, but only 37% said that the majority of oncologists they knew were skilled specialists. Finally, while 70.4% reported that they had a close working relationship with the palliative care services in their region, actual levels of collaboration were relatively low: only 37.8%

worked closely with a palliative care team, and only 35.1% and 33.3% regularly collaborated with a palliative care specialist or nurse, respectively.

Patient barriers have been identified as follows: reluctance to report pain because of the conviction that health professionals must not be distracted from dealing with the main problem, i.e. the tumor, that pain is innately related to the cancer and as such cannot be eliminated, and that the acknowledgement of a higher level of pain indicates awareness of disease progression; fear of not being considered a 'good patient'; reluctance in taking pain medications due to the well-known 'myths about opioids', represented by fear of addiction and/or of being thought of as an addict, fear of analgesic tolerance, and fear of side-effects. All these factors culminate in a 'willingness to put up with pain' and in a determination to take as few medications as possible, prolonging the 'use as needed' strategy and refusing an 'around the clock' type of administration [2, 12].

A correlation has been demonstrated between the level of pain reported by patients and the presence of these barriers, and specific training programmes have been hypothesized to help break down all the three typologies [12].

A recent systematic review of works evaluating the most effective interventions to improve cancer pain management in hospitalized patients highlighted a number of important strategies on the basis of professional (nurses only) and patient education, regular pain assessment (pain as a vital sign), audit of pain results and feedback to clinical staff, computerized decisional support systems, and referral to specialist-level pain and palliative care consultation services. While an improvement in intermediate outcomes (patient satisfaction, documentation of pain intensity, nurses' expertise, and attitudes) was obtained using such approaches, an improvement in pain control was only achieved through a collaboration with palliative care centers [16].

The work by Reid et al. [17], published in this issue of *Annals of Oncology*, reports the results from a qualitative study on the factors that influence a patient's decision to accept or refuse a strong opioid to treat cancer pain. The title of the paper, 'Symptom control for the living or comfort for the dying', would seem to indicate that the level of acceptance is influenced by the patient's conception of treatment with opioids. Although the work, at first glance, focuses on the above-mentioned patient and family barriers, it also provides an interesting insight into 'physician barriers'.

The patient setting is rather unusual in that it involves a population about to start treatment with opioids and randomized to receive weak or strong opioids. The authors identify four categories of difficulty in accepting strong opioid therapy: patients are reminded of their imminent death when strong opioids are proposed and some even fear that these drugs will hasten their death; morphine is considered as a last resort; the feeling of having no choice but to start treatment with strong opioids; the role of health-care professionals in dealing with these situations. Problems such as fear of addiction, tolerance, and side-effects are less evident in this population than in similar groups described in other studies [18]. These fears were studied and revealed by *ad hoc* instruments such as the Barriers Questionnaire II, on the

basis of the analysis of four factors: physiological effects, fatalism, communication, and harmful effects [18]. Reid et al. hypothesize that this discrepancy could be a consequence of the qualitative methods used in their study in which patients were not constrained by predefined items or categories.

It clearly emerges from the work that the way in which physicians broach the issue of starting opioid therapy, however, strongly influences the patient's decision, as does the existing relationship between physician and patient. Reid et al. [17] illustrate this point by commenting on a daughter who expresses her concern to her father's physicians that administering strong opioids could hasten his death. The physicians give the rather discomfiting reply that, in effect, such an intervention 'probably would kill him'. This indicates that even professional figures fall victim to 'the myths about morphine' despite overwhelming evidence of the safety of opioids, which is what should be focused on by physicians in an effort to reassure patients and their families. Before being able to adopt a positive approach when proposing an opioid treatment, a physician needs to be confident that treatment with opioids does not have a negative impact on survival, that the principle of double effect is not needed to justify this therapy from an ethical point of view, and that pain has an important antagonist effect on the modest respiratory depression of the drug [19, 20]. Furthermore, a recent review of literature reports that addiction to opioids is present in 0%–7.7% of cancer patients, depending on the subpopulation studied and on the evaluation criteria used [21]. Although this problem must be borne in mind and dealt with, when necessary, by an expert in the field, it should not become a reason for denying analgesic treatment to those who need it.

Some participants to the Reid's study did not even expect the issue of pain to be broached owing to the heavy workload of the staff, while others felt that the intensity of pain they reported was regarded by doctors with some disbelief. All patients, however, desired more appropriate and detailed information on opioid treatment. Above all, trust in health-care professionals was reported as an important factor in helping patients to decide about opioid therapy.

To sum up, professional competence, correct communication, and a relationship based on trust are the three principle factors taken into consideration by patients when deciding whether or not to start opioid treatment. If patients receive unspoken confirmation from physicians of their idea of opioids as 'a last resort' and of the fact that treatment is linked to prognosis rather than to severity of pain, their determination to refuse treatment will be reinforced from a theoretical point of view. If, on the other hand, limited confidence and skills are shown by doctors in managing opioid side-effects, patient refusal will take on empirical characteristics because of the ensuing damage they fear the drugs will cause. The importance for patients of having their pain acknowledged and, in a certain sense, 'legitimized' within the doctor–patient relationship, during any stage of the disease, cannot be stressed enough. It is known that a 'catastrophizing' strategy for coping with pain is linked to the patient's perception of how others respond to their

complaints of pain. The perception of incredulity of the pain reported, of an underestimation of its severity, and of inadequate social support can thus lead to an increase in the level of suffering and of its expression [22]. It has also been shown that a good doctor–patient relationship can influence patient suffering to the extent of substantially reducing requests to hasten death in cancer populations [23, 24].

From an organizational point of view, pain is treated during active therapy by the patient's oncologist in collaboration with a palliative care specialist, and this comanagement is destined, over time, to become continuous. Therefore, setting aside the diatribe as to who is best qualified to coordinate the care of advanced cancer patients, a model of simultaneous care is needed to guarantee continuity of care, flexible patient/disease management, and appropriate objectives in each single clinical situation. Successful examples of this type of care model can be seen in Departments of Oncology which have their own Palliative Care Unit and in the ESMO Designated Centers of Integrated Oncology and Palliative Care program [15, 25].

In conclusion, the study of Reid et al. [17], which originates from the birthplace of palliative care, is somewhat disturbing in the messages it conveys—extreme fear of opioids and high barriers to palliative care strategies. It indicates that a great many years of health education have not produced the results that might have been hoped for. The problem remains that a number of oncologists today still tend to reserve the use of opioids for the final stages of the disease. A vision of pain management and palliative care that is not solely linked to the end-of-life but rather seen as a positive option, in the less advanced stage of disease as well, needs to be promoted.

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